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10/580,029	05/19/2006	Yukako Fukuhira	Q95047	7517

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,029	FUKUHIRA ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-11* is/are pending in the application.

4a) Of the above claim(s) *5 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/2006;12/13/2006;12/31/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of February 11, 2008, to the Restriction Requirement dated January 10, 2008 has been entered. Claim 7 has been cancelled, and claim 1 amended. No claims were newly added. Claims 1-11 are pending in the Application.

Response to Election/Restrictions

Applicants' election of Group I (claims 1-10), drawn to a tissue regeneration substrate comprising a film with a honeycomb structure, comprised primarily of a polymer compound and a phospholipid, is acknowledged. Applicants' election of phosphatidylethanolamine as the species of phospholipid, is further acknowledged. The election was made without traverse.

Accordingly, claims 5 and 11 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions and species of invention, there being no allowable generic or linking claim.

As the restriction is still deemed proper, the requirement for restriction is maintained and hereby made FINAL. The instant claims have been examined commensurate with the scope of the elected invention and the species of the elected invention. Applicant timely responded to the restriction (election) requirement in the reply filed February 11, 2008.

Claims 1-4, 6 and 8-10 are under current examination.

Information Disclosure Statement

The information disclosure statements dated 5/19/2006, 12/31/2006 and 12/31/2007 have been considered and indicated as such on Forms PTO-1449.

Objection to Specification

The brief description of the drawings corresponding to Figures1 and 2 are objected to, because the Figures refer to items 1, 2, 3 and 4, that are not described in the brief description. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 8-10 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nishikawa et al. (Materials Sci. and Eng. C8-9: 495-500; 1999; of record), in view of Watanabe et al. (Biomacromolecules 3:1109- 1114; 2002; of record), and further in view of Sawhney, A. (U.S. Patent No.: 6,818,018; filed Aug. 14, 1998).

The claims embrace a tissue regeneration substrate comprising a film with a honeycomb structure having an average cavity inner diameter from 0.1 to 20 μm, composed primarily of a polymer compound and phosphatidylethanolamine.

Nishikawa et al. describe honeycomb-patterned thin films of amphiphilic co- polymers as cell culture substrates, that work as adhesive sites for the cells (Title and Abstract). The preparation of honeycomb films for cell culture substrates is described in section 2.2, p. 142. Nishikawa et al. describe determining the average diameter of honeycomb holes in section 2.3, p. 143, and observed that hole size of the honeycombs can be passively controlled by changing the cast volume of the polymer solution, the polymer concentration and the humidity of atmosphere, as well as the chemical properties of the polymer, exemplified by increasing the maximum diameter from 1.9 to 3.8 μm (second column, p. 144; first column p. 146; limitation of claim 1).

While Nishikawa et al. do not describe including a phospholipid to their polymer film, the use of phospholipid polymers for tissue engineering was well known in the prior art, as described by Watanabe et al., teaching a porous scaffold as a cell-compatible material composed

of a phospholipid co-polymer of poly (lactic acid) for tissue engineering (Title and Abstract). Thus, curing the deficiency of a phospholipid in Nishikawa et al., and providing the motivation to include phospholipid polymers in constructing honeycomb structured films as tissue substrates. As the disclosure of both Nishikawa et al. and Watanabe et al. are directed to porous tissue regeneration substrates, it would have been obvious to include the phospholipid described by Watanabe et al. in the co-polymer film of Nishikawa et al. (limitation of claim 9).

The phospholipid described in constructing the porous scaffold of Watanabe et al. is MPC, and not phosphatidylethanolamine. Sawhney et al. describe polymerizable hydrogels as matrices for carrying cells (Title and Abstract), comprising various polymers and lipids such as phosphatidylethanolamine (lines 35-36, column 12; limitation of claims 1, 3 and 4), that are further biodegradable (line 21, column 13; limitation of claim 2). Thus, curing the deficiency of phosphatidylethanolamine in Nishikawa et al. and Watanabe et al., and providing the motivation to include phosphatidylethanolamine as a phospholipid in their porous tissue regeneration complex. Sawhney et al. further describe using the hydrogel for tissue augmentation or implant for cartilage (lines 22-29, column 19; limitation of claims 8 and 10).

The teachings of Nishikawa et al., Watanabe et al. and Sawhney are all directed to polymeric scaffolds and complexes for tissue regeneration. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings to include phosphatidylethanolamine as a phospholipid in the honeycomb film cell substrate with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to augment the honeycomb film of Nishikawa et al. with a phospholipid, because such would provide a superior cell compatible phospholipid copolymer, that coupled with the biodegradable properties described by Sawhney, would produce a complex suitable for cell delivery and tissue regeneration.

Claims 1 and 6 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nishikawa et al. (Materials Sci. and Eng. C8-9: 495-500; 1999; of record), in view of Watanabe et al. (Biomacromolecules 3:1109- 1114; 2002; of record), and further in view of Sawhney, A.

(U.S. Patent No.: 6,818,018; filed Aug. 14, 1998), as applied to claims 1-4 and 8-10 above, and further in view of Zou et al. (U.S. Patent Publication No.: 2002/0187105; filed Feb. 1, 2002).

The claims embrace a tissue regeneration substrate comprising a film with a honeycomb structure having an average cavity inner diameter from 0.1 to 20 μm, composed primarily of a polymer compound and phosphatidylethanolamine, characterized in that the compositional ratio of the polymer compound and the phospholipid is 10:1 to 500:1 by weight.

Nishikawa et al. describe honeycomb-patterned thin films of amphiphilic co- polymers as cell culture substrates, that work as adhesive sites for the cells (Title and Abstract), with specific examples of 2.0 and 4.0 μm diameter (first column p. 145; limitation of claim 1).

While Nishikawa et al. do not describe including a phospholipid to their polymer film, the use of phospholipid polymers for tissue engineering is described by Watanabe et al., teaching a porous scaffold as a cell-compatible material composed of a phospholipid co-polymer of poly (lactic acid) for tissue engineering (Title and Abstract). Thus, curing the deficiency of a phospholipid in Nishikawa et al., and providing the motivation to include phospholipid polymers in constructing honeycomb structured films as tissue substrates.

Sawhney et al. describe polymerizable hydrogels as matrices for carrying cells (Title and Abstract), comprising various polymers and lipids such as phosphatidylethanolamine (lines 35-36, column 12; limitation of claim 1), that are further biodegradable (line 21, column 13). Thus, curing the deficiency of phosphatidylethanolamine in Nishikawa et al. and Watanabe et al., and providing the motivation to include phosphatidylethanolamine as a phospholipid in their porous tissue regeneration complex.

While Watanabe et al. and Sawhney et al. do not specify a compositional ratio of the polymer compound and the phospholipid as 10:1 to 500:1 by weight, Watanabe et al. simply describe including the desired amount of phospholipid in the polymer synthesis reaction (second column, p. 1110), highlighting the non-criticality in the amount of phospholipid added. The non-criticality of the claimed range is also evident by the fifty fold weight ratio difference instantly claimed, and the teachings of the instant specification, that include a 1000 fold weight ratio in a preferred embodiment, and further state: "the source of the phospholipid composing the film of the invention is not important, and the phospholipid may be one extracted from animal tissue or

one produced by artificial synthesis." (pp. 5 and 6). Applicants should further note that as indicated in MPEP 2144.05: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Nonetheless, Zou et al. describe polymeric combinations for delivery of therapeutically effective compositions (Title and Abstract), that include lipids, such as phosphatidylethanolamine (¶ [0124], p. 11), and wherein the ratio of lipid to polymer is the composition is from about 1:2 to 1:20 (i.e. equivalent to a 2:1 to 20:1 polymer to lipid ratio; meeting the limitation of claim 6).

The teachings of Nishikawa et al., Watanabe et al., Sawhney and Zou et al. are all directed to polymeric scaffolds and complexes. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings to include phosphatidylethanolamine as a phospholipid in the honeycomb film cell polymeric substrate in a 20:1 lipid to polymer ratio with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to augment the honeycomb film of Nishikawa et al. with a phospholipid, and would employ a 20:1 lipid to polymer ratio as a matter of design choice, because such would provide a superior cell compatible phospholipid copolymer, that coupled with the biodegradable properties described by Sawhney, would produce a complex suitable for cell delivery and tissue regeneration.

Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226

(Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-10 and 12 of copending U.S. Patent Application No.: 10/552,685 (Patent Publication No.: 2006/0189911; commonly assigned). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '568 Application are directed to a biodegradable film having a honeycomb structure comprising a biodegradable polymer and a surfactant that is a phospholipid (claim 4). The phospholipid is further disclosed as phosphatidylethanolamine (claims 9 and 10). Claim 12 of the '685 Application further discloses the ratio of polymer to phospholipid as 1/1 to 1,000/1, overlapping the instantly claimed ratio.

While the claims of the '685 Application do not specify that the honeycomb structure has an average inner diameter from 0.1 to 20 μm, the specification of the '685 Application discloses the same (¶ [0028] of the published Application).

It is noted that while the instant claims recite a tissue regeneration substrate comprising a film with a honeycomb structure composed primarily of a biodegradable polymer and a phospholipid, the claimed product cannot be differentiated from that of the '685 Application claims, as "tissue regeneration" is merely an intended use for the claimed product. Thus, the instantly claimed honeycomb film and the honeycomb film of the '685 Application cannot be structurally distinguished. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Therefore, to practice the instant invention, it would have been obvious to one of ordinary skill in the art that the honeycomb polymer/phospholipid film claimed in the '685 Application is reasonably embraced by the honeycomb polymer/phospholipid film in the instant claims because the structural elements of the compositions are indistinguishable. Thus, claims 4-10 and 12 of copending U.S. Patent Application No.: 10/522,685 and claims 1-4 and 6 of the instant application are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-4, 6 and 8-10 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633